



# HBOCs: The PolyHeme Study Did it work?

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### Disclaimer – no conflicts

# What is the problem?



# What is the problem?



• CDC: Trauma as the leading cause of death among Americans under age 45.

#### 5 Leading Causes of Death, United States

2004, All Races, Both Sexes

#### Click on any colored box for detailed causes and ICD codes.

Click on any age group for percentages.

	Age Groups										
Rank	<u>&lt;1</u>	<u>1-4</u>	<u>5-9</u>	<u>10-14</u>	<u>15-24</u>	<u>25-34</u>	<u>35-44</u>	<u>45-54</u>	<u>55-64</u>	<u>65+</u>	All Ages
1	Congenital Anomalies 5,622	<u>Unintentional</u> Injury <u>1,641</u>	<u>Unintentional</u> Injury <u>1,126</u>	<u>Unintentional</u> Injury <u>1,540</u>	Unintentional Injury 15,449	<u>Unintentional</u> Injury <u>13,032</u>	<u>Unintentional</u> Injury <u>16,471</u>	Malignant Neoplasms 49,520	Malignant Neoplasms 96,956	Heart Disease 533,302	Heart Disease 652,486
2	Short Gestation 4,642	Congenital Anomalies 569	Malignant Neoplasms 526	Malignant Neoplasms 493	<u>Homicide</u> <u>5,085</u>	<u>Suicide</u> <u>5,074</u>	Malignant Neoplasms 14,723	Heart Disease 37,556	Heart Disease 63,613	Malignant Neoplasms 385,847	Malignant Neoplasms 553,888
3	SIDS 2,246	Malignant Neoplasms 399	Congenital Anomalies 205	<u>Suicide</u> 283	<u>Suicide</u> <u>4,316</u>	<u>Homicide</u> <u>4,495</u>	Heart Disease 12,925	<u>Unintentional</u> Injury <u>16,942</u>	Chronic Low. Respiratory Disease 11,754	Cerebro- vascular 130,538	Cerebro- vascular 150,074
4	Maternal Pregnancy Comp. 1,715	<u>Homicide</u> <u>377</u>	<u>Homicide</u> <u>122</u>	<u>Homicide</u> <u>207</u>	Malignant Neoplasms 1,709	Malignant Neoplasms 3,633	<u>Suicide</u> <u>6,638</u>	Liver Disease 7,496	Diabetes Mellitus 10,780	Chronic Low. Respiratory Disease 105,197	Chronic Low. Respiratory Disease 121,987
5	Unintentional Injury 1,052	Heart Disease 187	Heart Disease 83	Congenital Anomalies 184	Heart Disease 1,038	Heart Disease 3,163	HIV 4,826	<u>Suicide</u> <u>6,906</u>	Cerebro- vascular 9,966	Alzheimer's Disease 65,313	Unintentional Injury 112,012

# What is the current prehospital fix for trauma?







# What is the REAL fix?

### Blood, a trauma center and a Surgeon





# PolyHeme®

 cross-linked polymer of human Hb in which two or more tetramers are covalently linked.



# What is hemoglobin?



# **New Resuscitation Paradigm**



- 32 Level 1 Trauma Centers
- 150 Physician Investigators
- 3500 EMT Paramedics
- 300 EMS vehicles

USA Multicenter PolyHeme Resuscitation Trial

### **Study Objective**

To determine survival of patients in hemorrhagic shock treated with:

**PolyHeme or Standard of Care** 



# Study Design: Prehospital

# Severely injured trauma patients were assigned to one of two groups by chance





Test (PolyHeme®)

(Case)

**Receive IV PolyHeme** 

Standard of Care (Control)

**Receive IV Salt Water** 



# Enrollment

### **PolyHeme Resuscitation Trial**

<b>Study Entry</b> ( Prehospital )	<b>POLYHEME</b> ( n = 350 )	<b>CONTROL</b> ( n = 364 )
Age (±SEM) – years	36 <u>+</u> 0.8 ←	→ 38 <u>+</u> 0.9
Male	78 %	<b>→</b> 79 %
Penetrating	53 % 🔶	<b>→</b> 52 %
SBP (±SEM) – mmHg	78 <u>+</u> 0.7 ←	<del>78 <u>+</u> 0.6 +</del>
ISS (±SEM)	20 <u>+</u> 0.8 ←	→ 19 <u>+</u> 0.7
Transport time – min	26	26





# **Protocol Violations**

- 124 Patients.
  - 71 in the PolyHeme Group
  - 53 in the Control group
- Some shouldn't have been enrolled
  - No blood pressure in field
  - Head injury or abnormal brain function
  - Undergoing CPR
- Did not receive the assigned treatment

# **Results: Protocol Followed Correctly**





# Primary Outcome Measure

**Efficacy : Day 30 Mortality** 

Study Group	As Randomized ( n = 714 )	<b>As</b> <b>Treated</b> ( n = 714 )	Per Protocol ( n = 590 )
POLYHEME	<mark>13 %</mark>	<mark>13 %</mark>	<mark>11 %</mark>
	( 47 / 350 )	( 46 / 349 )	( 31 / 279 )
CONTROL	10 %	<mark>10 %</mark>	<mark>9 %</mark>
	( 35 / 364 )	( 36 / 365 )	( 29 / 311 )

p = NS for all treatment comparisons



Secondary Endpoint							
<b>PolyHeme Resuscitation Trial :</b>							
Safety Analysis							
<b>Adverse Event</b> ( Reported by the PI )	<b>POLYHEME</b> ( n = 349 )	<b>CONTROL</b> ( <b>n</b> = 365 )	р				
Adverse Events ( AEs )	324 = <b>93%</b>	322 = <b>88%</b>	0.04				
Serious Adverse Event ( SAEs )	141 = $40\%$	126 = 35%	NS				

# Study Implications: Benefit-to-Risk

- PolyHeme intended for use in bleeding patients without early access to blood
  \*\*\* Not in place of blood \*\*\*
- Benefit-to-risk considerations
  - Patients at risk of dying
  - High mortality without blood
  - No available alternative carries oxygen

# Conclusion

## PolyHeme can provide a survival benefit to bleeding patients without access to blood



### Next Step

# Submission to the FDA for product approval.

**Future Issue: Permissive Hypotension** 



# Questions?



# **PolyHeme Investigators**

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